Council for Responsible Nutrition
1828 L Street, NW, Suite 900 • Washington, DC 20036-5114
(202) 776-7929 • fax (202) 204-7980 • www.crnusa.org

May 2, 2008

Fran Kammerer
Staff Counsel
Office of Environmental Health Hazard Assessment
1001 I Street
Sacramento, CA 95812
Filed via e-mail: fkammerer@oehha.ca.gov

Re: Comments to the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, on the "Request for Public Participation, Notice of Public Workshop – Proposition 65 Regulatory Update Project, **Beneficial Nutrients Regulatory Concept**" [3/21/08]

Dear Ms. Kammerer:

These comments are filed on behalf of the Council for Responsible Nutrition (CRN), the leading trade association representing dietary supplement manufacturers and ingredient suppliers. CRN companies produce a large portion of the dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug store and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies.

The OEHHA Regulatory Concept Draft is an effort to reconcile the need for foods (including ordinary foods, fortified foods, and dietary supplements) to provide essential and beneficial nutrients with the responsibilities of OEHHA under Proposition 65 to develop and administer regulations that fulfill this objective. To that end, OEHHA provided a brief discussion of the background and rationale, proposed a Possible Regulatory Concept, Section 1250X, and set schedules for a public workshop (April 18, 2008) and written comments (May 2, 2008) on this topic. Nevertheless, CRN is concerned that this project is misdirected. We believe, as will be demonstrated below, that the proposal is unnecessary, misunderstands the purposes and limitations of Recommended Daily Allowances (RDAs) and Upper Levels (ULs) and blurs the distinction between essential and beneficial nutrients on the one hand and arbitrarily assigned values for what constitutes an exposure on the other without regard to relevant risk assessment data. In addition, we are concerned by comments made by OEHHA staff at the public workshop on April 18, 2008 that the agency did not intend the proposal to apply to dietary supplements. CRN respectfully requests that OEHAA withdraw this Concept Draft and terminate this project.

CRN is submitting these comments to help assure that that the scientific and legal issues behind the OEHHA proposal are fully considered. Specifically, the comments will examine the risk assessment principles and data that should underlie the identification of any labeling thresholds for vitamins, minerals or other nutrients that have been officially identified by OEHHA as carcinogens (CARCs) or developmental or reproductive toxicants (DARTs).

Summary of Major Concerns

1. The proposal is unnecessary because retinol, the only nutrient listed as a CARC or DART under Proposition 65, already has an assigned threshold which consititues an "exposure."

2. The term "food" must be understood, if this proposal moves forward, to include dietary supplements as a subcategory of food, as required under the Federal Food, Drug and Cosmetic Act.

3. The proposed quantitative thresholds are scientifically invalid, unnecessarily restrictive, and internally inconsistent.

4. The assigned values for Recommended Dietary Allowances (RDA) and Daily Values (DV) are unrelated to safety, and thus are invalid as Proposition 65 labeling thresholds.

5. The proposed risk-based 20% of the Upper Level (UL) is an arbitrary determinations that leads to conservative and overly restrictive values for some nutrients.

1. <u>OEHHA's Proposal With respect to Beneficial Nutrients is Unnecessary</u>

Under California law, a need for the unilateral administrative actions must be demonstrated. Given the history of Proposition 65 and the manner in which it has addressed specific nutrients for possible listing to date, it is hard to understand why this proposal is needed. Since Proposition 65 was enacted over 20 years ago, only two chemicals with possible nutrient applications have been listed and both have resolved the potential conflict through careful description of the chemical being listed. Retinol is the only nutrient listed as a CARC or DART that in the same form also constitutes an essential nutrient. It was addressed through qualification of that listing in 1989, which states:

> Retinol/retinyl esters, when in daily dosages in excess of 10,000 IU, or 3,000 retinol equivalents. (NOTE: Retinol/retinyl esters are required and essential for maintenance of normal reproductive function. The recommended daily level during pregnancy is 8,000 IU.)

Likewise, when Chromium was listed in 1987, the scientific panel again carefully described the listed chemical as "chromium (Hexavalent compounds)" so as to distinguish the chemical being listed from the one recognized as a beneficial nutrient. Chromium is a nutrient only at a valence of 3+. Chromium is listed under Proposition only for the 6+ form, which is not the nutrient. After much scientific investigation, there is no evidence whatever that any biological system converts Cr 3+ to Cr 6+, and therefore the nutritive forms of chromium are not listed under Proposition 65. This approach of carefully defining the listed chemical is a more precise and more appropriate manner to address the possible listing of a beneficial nutrient should any others be considered in the future. Thus it is hard to see why this proposal is needed at all.

2. <u>"Food" Includes Dietary Supplements</u>

If, however, OEHHA does decide to proceed with this concept to a formal rulemaking proposal, it should expressly state that the term "food" includes dietary supplements as a subcategory of "food" as specified by the Federal Food, Drug and Cosmetic Act. CRN was dismayed to learn at the public workshop that OEHHA staff did not interpret dietary supplements as food. This is not supported by either plain reading the federal law, or the practical effects of such an interpretation.

The federal Food, Drug and Cosmetic Act defined food as "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article." 21 U.S.C. 321 (f). This is a broad definition encompassing food in all its forms. A dietary supplement is defined in that same Act, in relevant part, as follows:

The term 'dietary supplement' ---

(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;
(B) a mineral;
(C) an herb or other botanical;
(D) an amino acid;
(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);

(2) means a product that--

(A)(i) is intended for ingestion in a form described in section 350(c)(1)(B)(i) of this title; or (ii) complies with section 350(c)(1)(B)(ii) of this title;
(B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and
(C) is labeled as a dietary supplement; . . .

[additional material omitted]

> **Except for purposes of paragraph (g), a dietary supplement shall be deemed to be a food within the meaning of this chapter.** 21 U.S.C. 321(ff). *(emphasis supplied)*

As is made clear by the final sentence of the definition, dietary supplements, under the federal Food, Drug and Cosmetic Act are deemed to be a food unless expressly and specifically identified for separate treatment under the law.

As a practical matter, beneficial nutrients are provided in both "traditional food" (as OEHHA perceived that term) and in dietary supplements. Indeed, in today's marketplace of fortified foods, nutrient-enriched drinks and snacks, and "functional foods" – a marketplace term referring to food products marketed specifically for their nutritive value – consumers have the choice of how to achieve their optimal nutrition. A "traditional food" might include the exact same essential and beneficial nutrients in identical levels of a multivitamin or other dietary supplement, but under the interpretation proposed by OEHHA, the "traditional food" would not constitute an exposure (thereby avoiding the Prop 65 warning on a product containing that nutrient), but the nutrient in the dietary supplement would trigger the mandatory Proposition 65 warning. Such a result does not advance the purposes of Proposition 65; unfairly singles out dietary supplements for disparate treatment; and confuses consumers as to which products actually present potential exposures to listed chemicals.

Thus, if this proposal should advance to a rulemaking, OEHHA should make clear that dietary supplements are included as "foods".

3. The Quantitative Thresholds for RDAs and UL Are Misguided

Although Proposition 65 does not authorize the removal of any products or ingredients from the marketplace, the purpose of this law is unequivocally related to safety issues and providing consumers with notice of products that may contain chemicals determined by the State of California as hazardous. Warnings may be required under Proposition 65 only if OEHHA has identified a substance as a CARC or a DART, both of which are toxic actions that have major adverse health consequences, and only if the established quantitative thresholds for that chemical are exceeded.

OEHHA's concept draft appears to try to accomplish the following: Proposition 65 requires warnings for any exposure to a listed chemical for purposes of the Safe Drinking Water and Toxic Enforcement Act of 1986. OEHHA's proposal would re-define "exposure" to omit any food containing that chemical if it is a beneficial nutrient[1] that

[1] In general, IOM's DRI documents do not define or describe "beneficial nutrients." The term is redundant. A substance must be beneficial to be a nutrient. On the other hand, IOM recognizes that some nutrients are essential (e.g., retinol, ascorbic acid, calcium, and iron), while others are clearly non-essential (e.g., glucose and sucrose) but are nonetheless "beneficial" (e.g., the carbohydrates provide energy).

does not exceed the RDA for that nutrient, or if no RDA is established, that does not exceed 20% of the UL for that nutrient. Thus, the proposed OEHHA inquiry may not be a safety assessment of the chemical at all for purposes of determining what requires a warning and what doesn't – rather it appears to be a determination by OEHHA that if the nutrient does not exceed the RDA as determined by the federal government, then it should be exempt from Prop 65 labeling. If no RDA is established, then the chemical similarly is exempt from labeling if it does not exceed 20% of the UL.

4. Neither the RDA nor the Daily Value Is an Appropriate Measure of Optimal Nutrition

The flaws with this analysis are many: First, it assumes that the RDA is the level at which the nutrient ceases to be beneficial, or even that the RDA is the "optimal' level at which the nutrient is beneficial. In fact, neither is correct. While the RDA[2] (determined by the Institute of Medicine's Food & Nutrition Board), and even the Daily Value[3] ("DV", set by FDA) are intended as markers for the beneficial effects of nutrients; neither value is based on the avoidance of adverse effects of excessive intakes and thus, neither is valid as a threshold for avoiding carcinogenic or developmental or reproductive risks. The RDA is the recommended amount to avoid nutrient related deficiencies. Many nutrients (e.g., Vitamin C) show beneficial health effect at levels far above their RDA, and some health benefits may not even be present at the RDA level but are apparent only at higher levels. In addition, not all nutrients have an RDA (e.g., vitamin D and calcium have "Acceptable Intakes"— see footnote 1) or Daily Value (e.g., all individual amino acids) established, and any Proposition 65 warning that might be required in the future could not be based on these values.

RDA and DV are conceptually and quantitatively invalid as the basis for warning thresholds related to toxic effects. Nor are they appropriate levels to set as a matter of public policy for establishing what levels of a nutrient are "beneficial" (and thus, should justify an exemption from warning).

---

[2] The RDA acronym is derived from Recommended Dietary Allowances, one of the four values of the Dietary Reference Intakes (DRI) system by the Institute of Medicine. The IOM sets RDA values only for nutrients for which it can identify an *average* requirement, the Estimated Average Requirement (AER). When an EAR is identified, the RDA is calculated as RDA = EAR + 2 Standard Deviations. When no EAR can be identified, the IOM set an Acceptable Intake (AI) that is an amount that accomplished the recognized beneficial effects in the test population. When no RDA is set, the AI is used in a similar manner. The OEHHA statements do not clarify what use would be made for the AI under the proposed new regulatory language, Section 1250X.

[3] The Daily Value (DV) is established by the US Food and Drug Administration through the rulemaking procedure to serve as the basis for percentage calculations for use on food labels, including those of dietary supplements. The DV are not necessarily related to the most recent of the RDA or AI values from the IOM. It must be recognized, however, that the RDA (or AI, but never both for the same nutrient at the same time) and DV describe or relate to nutritional benefit and need, but not safety. The fourth of the DRI values set by the Institute of Medicine, the Upper Level (UL), describes amounts known to be safe, and it is the only one of the four that does so.

Moreover, nutritional benefit is a proper qualification for deciding whether a substance produces an "exposure" under Proposition 65 when consumed at beneficial levels of intake, but it is not an appropriate criterion for deciding the quantitative level that would trigger the requirement for a warning label. Because the only biological effects that will cause a substance to be listed under Proposition 65 are toxic actions, the only scientifically valid approach to establishing quantitative thresholds for warnings is risk assessment. Assessment of nutritive or other benefits is neither required nor permitted in the identification of such thresholds. Which leads to OEHHA's alternative method of calculating "beneficial" – the use of the Upper Level (UL):

5. The "20% of Upper Level" Test is An Arbitrary Method to Set A Safe Amount of A Nutrient

In those cases in which there is no RDA, OEHHA proposes to establish the threshold level of a chemical to avoid "exposure" as 20% of the Upper Level (UL). The UL is based on safety considerations, but for most nutrients, the UL values have been established in relation to effects other than CARC and DART actions. It is conceptually possible that a substance might have a CARC or DART effect at the point of the UL, but many ULs are based on other, non-CARC or non-DART-related effects. For example, if niacin were to be listed under Prop 65 in the future, the current UL for niacin is based on a minor nuisance action—vasodilative flushing, and not on a serious toxic effect. In any such cases, the UL would not be valid as a threshold for warnings related to CARC or DART risk because the type of effect considered in setting the UL is not related to CARC or DART actions.

The selection of 20% of UL as the Proposition 65 warning threshold is even more arbitrary. It just happens that the RDA for retinol (the only nutrient currently listed under Proposition 65) is 20% of the UL -- but that is not generalizable to other nutrients. If other nutrients were to be identified as CARC or DART in the future, the percentage of the UL that would be equivalent to the RDA would likely be different for each. For selenium, 20% of the UL is nearly double the RDA; and for vitamin E, 20% of the UL is 30 times the RDA. Thus, these examples demonstrate that percentage of the UL should not be set at 20% but should vary on a case-by-case basis.

Regardless of any comparison to the RDA, the current example of retinol demonstrates that a threshold of the 20% of the UL is unnecessarily restrictive. The original labeling threshold of 10,000 IU for labeling of retinol in relation to its well-known DART effects was appropriate. Although this level was established by OEHHA many years before the US Institute of Medicine (IOM) published the Tolerable Upper Intake Level (UL) concept and established UL values for many nutrients, the 10,000 IU threshold is prescient—it exactly matches the UL established later by IOM. Moreover, the IOM UL for retinol is based on the avoidance of risk of birth defects, and thus, is consistent with one of the two toxic effects at issue under Proposition 65.

The most important point, however, is that there is no history whatsoever of products containing 10,000 IU or less retinol causing DART effects in any US area or population group. Thus, there is no public health justification for lowering the retinol threshold from its current level that is equivalent to 100% of the UL to 20% of the UL. The suggested 20% of UL threshold is not justified on the basis of any toxicological and risk assessment considerations. From the retinol example, the labeling requirement should be triggered at 100% of the UL if the UL is set on the basis of a CARC or DART action. If the UL is set on the basis of some other toxic effect, the Proposition 65 labeling decision should be based on a risk assessment on the CARC or DART data.

Conclusion

The concept draft by OEHHA lacks clarity and specificity to establish with accuracy the "beneficial" levels of nutrients so as to exclude them from mandatory labeling under Prop 65. While OEHHA's apparent purpose– to avoid consumer confusion over chemicals in foods that are both well-recognized nutrients, and at the same time, potential targets for listing under Prop 65 – is laudatory, this proposal fails to appreciate the federally-developed values on which it would base those determinations. Indeed, California has been well-served over the past twenty years by the careful description of such chemicals on a case-by-case basis when they are listed (e.g., retinol). CRN respectfully suggests that OEHHA should abandon this effort and continue to rely on that case-by case approach. We appreciate this opportunity to provide OEHHA with our views.

Sincerely yours,

John Hathcock, Ph.D.
Senior Vice President, Science & International Affairs

Steven Mister, Esq.
President and Chief Executive Officer